Journal of Basic Research in Medical Sciences

Journal HomePage : https://jbrms.medilam.ac.ir

Ilam University of Medical Sciences Publications

Biochemical and Biological Properties of Curcumin and its Association with Carbohydrate Metabolism: A Review Article

Ali Nosrati Andevari [1], **Najmeh Ebrahimzadeh Shahandashti** [2], **Mohsen Koolivand** [3], **Faegheh Bahri** [1], **Rana Douseh** [4], **Durdi Qujeq** [5,6]✉

[1] Department of Clinical Biochemistry, Afzalipour Faculty of Medicine, Kerman University of Medical Sciences, Kerman, Iran
[2] Department of Medical Laboratory Science, Babol Branch, Islamic Azad University, Babol, Iran
[3] Royan Stem Cell Technology Company, Tehran, Iran
[4] Department of Pharmacology and Toxicology, School of Medicine, Babol University of Medical Sciences, Babol, Iran
[5] Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
[6] Department of Clinical Biochemistry, School of Medicine, Babol University of Medical Sciences, Babol, Iran

Article Info

Article type:
Review Article

Article History:
Received: Aug. 30, 2025
Revised: Feb. 17, 2026
Accepted: Apr. 06, 2026
Published Online: Jun. 16, 2026

✉ ***Correspondence to:***
Durdi Qujeq
Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

Email:
d.qujeq@mubabol.ac.ir

A B S T R A C T

Introduction: Carbohydrates, popularly known as sugars, are one of three major macromolecules essential for the functioning of living organisms. Altered carbohydrate metabolism can lead to the development of type 2 diabetes mellitus (T2DM). Uncontrolled blood glucose in T2DM is a risk factor for several serious complications, including cardiovascular and cerebrovascular disease, nephropathy, retinopathy, and neuropathy. Synthetic pharmaceuticals are often used by subjects with T2DM to reduce these risks. However, natural compounds from plants might be good candidates for enhancing carbohydrate metabolism and for the improvement of glycemic control.

Aim: The present study was aimed at assessing the biochemical and biological properties of curcumin with special reference to carbohydrate metabolism.

Discussion: Curcumin is the yellow pigment and the most important bioactive component of turmeric, which is obtained from the rhizomes of this medicinal plant. It has unique biological and structural features and variable bioavailability. The positive physiological effects of curcumin depend on the dose and the time of administration. Recently, curcumin nanoformulations have been proposed as novel therapeutic modalities to improve their bioavailability and clinical efficacy. Curcumin has structural properties that allow it to penetrate cells easily and exert beneficial metabolic effects by improving insulin secretion and sensitivity via modulation of glucagon-like peptide-1 (GLP-1), lipid metabolism, and inflammatory signaling pathways. Preclinical studies and randomized controlled trials (RCTs) have shown that curcumin is significantly associated with pathways involved in carbohydrate metabolism.

Conclusion: The available evidence suggests that curcumin may significantly improve carbohydrate metabolism and glycemic control in patients with type 2 diabetes mellitus. Curcumin, with its antioxidant, anti-inflammatory, and insulin-sensitizing properties, may be a promising natural therapeutic agent for the management of impaired glucose metabolism. But we need large clinical trials to prove that it works in the long run, at the right dose, and is safe.

Keywords: Curcumin, Turmeric, Carbohydrate, Glycemic, T2DM, Preclinical, RCT

➢ **Cite this paper**
Nosrati Andevari A, Ebrahimzadeh Shahandashti N, Koolivand M, Bahri F, Douseh F and et al. Biochemical and Biological Properties of Curcumin and its Association with Carbohydrate Metabolism: A Review Article. *J Bas Res Med Sci*. 2026; 13(3):60-72.

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

© Author(s) retain the copyright

Publisher: Ilam University of Medical Sciences

Introduction

Carbohydrates, or sugars, are one of three major classes of macromolecules required for physiological functions in living organisms (1). Carbohydrates are important for providing energy so cells can work. They exist in simple forms like glucose and fructose and in complex forms like sucrose and starch (2). Carbohydrate metabolism disorder is the primary cause of type 2 diabetes mellitus (T2DM). It comprises the majority of the cases of diabetes mellitus. This is usually the result of either inadequate insulin secretion or a reduced ability of the body to use insulin effectively (3, 4). Uncontrolled T2DM is associated with several complications such as cardiovascular and cerebrovascular diseases, nephropathy, retinopathy and neuropathy (5-7). Synthetic medications are usually used by subjects with T2DM to attenuate diabetic complications. These medicines have therapeutic benefits, but can also produce a range of adverse effects and may worsen blood glucose levels. Thus, natural compounds obtained from plants are a promising alternative to improve glycaemic control and increase carbohydrate metabolisms.

Curcumin is a yellow pigment and the main active ingredient of turmeric, obtained from the rhizomes of the medicinal plant (8). The present study explored the biochemical and biological properties of curcumin and its role in carbohydrate metabolism. Moreover, it aims to determine whether the results of the current study can be a basis for a systematic review and meta-analysis to explore the association of curcumin and carbohydrate metabolism in future studies.

This article is a narrative review, and the databases used were Google Scholar, PubMed, and Scopus. Most of the studies analysed were published in the period 2010–2025. Articles published before 2010 are less frequently used. The keywords were curcumin, carbohydrate, T2DM, FBS, FPG, insulin, HOMA-IR, FFA, DAG, cholesterol, IRS, PKC, PPAR, AMPK, TNF-α, IL-1β and TLR4. Most of the studies included in this narrative review were mainly research articles of preclinical and randomised controlled trial (RCT) phases. However, only a few review articles were analysed. A total of about 100 articles were screened; similar articles were excluded, and about 76 articles were selected to include in the final analysis.

Biochemical and Biological Properties of Curcumin

Curcumin is a bioactive compound with a specific molecular structure and biological properties as well as excellent bioavailability. The therapeutic effect of the compound is highly dependent on dose and time. The biological actions of curcumin include several physiological processes and chemical reactions in the body. Structurally, curcumin consists of two phenolic rings connected by an aliphatic chain, making it a bis-α,β-unsaturated β-diketone, known as 'diferuloylmethane', and has the chemical formula $C_{21}H_{20}O_6$ (9-11). Curcumin is generally available as a yellow powder; the colour is due to its β-diketone structure. This characteristic hue is significantly contributed by the electron-conjugated system. This yellow pigment can be easily detected at high concentrations (12). Curcumin is soluble in organic solvents like acetone, methanol, ethanol and dimethyl sulfoxide (DMSO). But it is poorly soluble in water. This solubility profile has a major effect on its absorption and bioavailability in the human body (10, 13). Curcumin has been chemically modified in different light, temperature and pH, which can lead to degradation. Therefore, the stability of this theory in different formulations should be carefully examined (14). For example, curcumin's chemical structure can be destabilised by acidic, alkaline or ultraviolet light (15). Moreover, oxidative reactions are also important in the degradation of curcumin, and bicyclopentadione was identified as the major product of oxidative degradation (16). High temperatures favour the degradation of curcumin and thus decrease its therapeutic efficacy (17). The

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

presence of excess moisture or water influences the stability of curcumin, and it can be degraded by oxidation and hydrolysis under humid conditions (18). Curcumin can be made more stable in neutral pH, storage in light-protected environments or opaque packaging, low and stable temperature, non-oxidative conditions or vacuum packaging techniques, dry environments and incorporation of nanoparticle technologies. Moreover, curcumin possesses an interesting property of a colour change from yellow in acidic conditions to red-orange in alkaline conditions at a pH of 8.5 or higher. This colour change is due to the protonation of curcumin, which transforms it from the keto (yellow) to the enol (red) form (19). Commercial curcumin contains about 77% diferuloylmethane, 17% dimethoxycurcumin and 6% bisdemethoxycurcumin (20). Curcumin has low bioavailability when taken orally. The bioavailability of substances such as curcumin in oral delivery systems comprising bioactive compounds is restricted by processes such as absorption, metabolism, distribution and excretion. However, the limited bioavailability of curcumin may not be an important issue because daily ingestion of high-dose curcumin may be beneficial to health. However, it is worth mentioning that long-term use of high-dose curcumin may lead to side effects, which can diminish its therapeutic benefits (21). Moreover, curcumin nanoformulation is proposed as a new therapeutic strategy to enhance the clinical effectiveness of curcumin. This method improves the aqueous solubility and can be targeted to specific tissues, which improves bioavailability, increases drug delivery efficiency and accelerates therapeutic outcomes (22). There are various methods of synthesis of nanocurcumin, like the Fessi method, nanoprecipitation, thin film hydration, microemulsion, emulsion polymerisation, ultrasonication, wet milling, spray drying, antisolvent precipitation, ionic gelation, solvent evaporation, coacervation, single emulsion and solid dispersion. These techniques have resulted in the development of different curcumin-based nanoformulations, such as micelles, liposomes, cyclodextrins, conjugates, and nano- or nanosphere structures (23). Piperine is the major bioactive compound of black pepper and accounts for most of its medicinal effects (24). Co-administration of curcumin with piperine improves the intestinal absorption of curcumin and inhibits its rapid hepatic metabolism, thus significantly increasing its bioavailability (25, 26). Hosseini et al. announced that fasting blood sugar (FBS) levels were significantly reduced in patients with T2DM and hypertriglyceridemia with the curcumin-piperine complex (27).

After absorption, curcumin undergoes a series of hepatic biotransformation processes. It is carried to the liver, where it is converted into several derivatives. Phase I and II metabolism of curcumin has been confirmed by both in vivo and in vitro studies. In phase I, the four double bonds of the heptane-3,5-dione system are sequentially reduced, yielding primary metabolites such as tetrahydrocurcumin and hexahydrocurcumin, while dihydrocurcumin and octahydrocuminol (also known as hexahydrocurcuminol) are formed to a lesser extent. The main enzyme in phase I metabolism is alcohol dehydrogenase. In phase II, the conjugation of the reduced metabolites takes place to form monoglucuronide, monosulphate and mixed sulphate/glucuronide derivatives (28) (Figure 1).

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

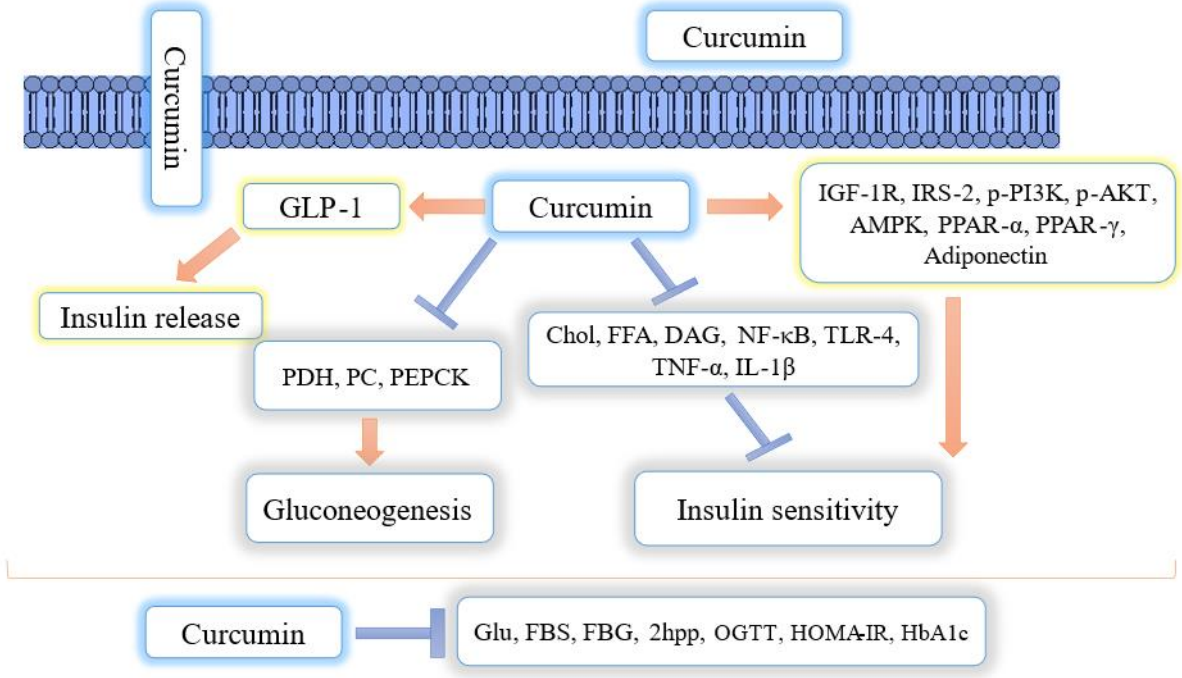

Figure 1. The effects of curcumin on sugar metabolism. Curcumin increases insulin secretion and sensitivity by acting on GLP-1, lipid metabolism, and inflammatory factors, thereby improving metabolism and glycemic indices. GLP-1: glucagon-like peptide-1, IGF-1R: insulin-like growth factor-1 receptor, IRS: insulin receptor substrate, PPAR: proliferator-activated receptor, PDH: pyruvate dehydrogenase, PC: pyruvate carboxylase, PEPCK: phosphoenolpyruvate carboxykinase.

Discussion

Curcumin's Relationship with Carbohydrate Metabolism

The interlinked metabolic pathways are aggravated by carbohydrates, as mentioned earlier, causing diabetic complications. Elevated glucose levels and accumulation of secondary and advanced products of carbohydrate metabolism result from impaired insulin secretion and signalling (29). The following sections discuss the mechanisms and agents that influence curcumin's effects on carbohydrate metabolism.

Curcumin effects on carbohydrate metabolism with involvement of lipids

The influx of pancreatic β-cells is caused by an increase in serum low-density lipoprotein cholesterol (LDL-C). These molecules accumulate intracellularly and interfere with insulin secretion (30). Curcumin has a significant effect on cholesterol and LDL-C reduction (31, 32). Curcumin may therefore stimulate the secretion of more insulin. Increased cellular cholesterol levels lead to accumulation of cholesterol in the cell membrane and attenuation of membrane fluidity. This leads to mislocalisation of insulin receptor subunits and associated adaptor proteins, resulting in impaired insulin signalling (33). Increased triglyceride (TG) levels are associated with increased free fatty acid (FFA) and metabolite synthesis rates, including diacylglycerol (DAG). These FFAs and DAGs impair the function of the insulin receptor substrate (IRS) and decrease insulin sensitivity by activation of protein kinase C (PKC) (34, 35). PKC activation is a major contributor to insulin resistance in diabetic states. Su et al. demonstrated that curcumin significantly decreased FBG, LDL-C, and FFAs in rat models of T2DM (36). Furthermore, Wang et al. also demonstrated that curcumin enhanced insulin signalling by up-regulating the expression of proteins like insulin-like growth factor-1 receptor (IGF-1R), IRS-2, phosphoinositide 3-kinase (PI3K), phosphorylated

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

PI3K (p-PI3K), Akt, and phosphorylated Akt (p-Akt) in the brains of APPswe/PS1dE9 mice (37).

The insulin signalling pathway influences cholesterol metabolism. Insulin suppresses FoxO1 activity in the liver, reduces the amount of 12α-hydroxylated bile acids, disrupts cholesterol absorption, and thus reduces plasma cholesterol levels in mice with hepatic deletion of the insulin receptor (38), as reported by Semova et al. Shao and colleagues showed that curcumin can improve insulin signalling in adipose tissue and hepatocytes. In addition, it downregulated hepatic lipogenic genes in C57BL/6J mice fed with either a low-fat or high-fat diet (HFD) (39).

Peroxisome proliferator-activated receptor gamma (PPARγ) is highly expressed in macrophages in adipose tissue (40). Activation of PPARγ increases insulin sensitivity by increasing the secretion of adiponectin (41). Thus, PPARα, PPARγ and adiponectin stimulate β-oxidation of FFAs (42, 43). Also, they greatly reduce the activation of PKC. Zhao et al., in their study, showed that curcumin improved insulin resistance in HFD rats by upregulation of PPARα and PPARγ (44). Demir et al. observed that curcumin at a 50 mg/kg/day dose increased the transcript levels of PPARα and PPARγ in Wistar albino rats (45). Moreover, Gao et al. demonstrated that the expression of PPARγ was enhanced in mouse Raw264.7 macrophages treated with curcumin (46). Adenosine monophosphate-activated protein kinase (AMPK) is an important regulator of fatty acid oxidation. Kim et al. (47) showed that curcumin increased glucose uptake in rat L6 myotubes through the activation of the AMPK-p38 MAPK signalling pathways.

Curcumin has been shown in studies to suppress glucose production. Wang et al. found that curcumin suppressed mitochondrial oxidation, thereby restricting the uptake of FFAs and inhibiting the accumulation of acetyl CoA, leading to reduced lipid accumulation. Therefore, curcumin preserved the activity of pyruvate dehydrogenase (PDH) but inhibited the activity of pyruvate carboxylase (PC) (48). Fujiwara et al. (49) reported that curcumin inhibited the hepatic gluconeogenesis by activating AMPK and inhibiting the activities of glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK).

Other studies on effects of curcumin on glycaemic indexes

The homeostasis model assessment of insulin resistance (HOMA-IR) is a validated method (50) to quantify insulin resistance. This metric enables the evaluation of metabolic function, particularly in subjects at risk of T2DM and other metabolic diseases (51). Huang et al. (52) reported that curcumin significantly improved HOMA-IR in T2DM rat models. In an RCT by Thota et al. (53), curcumin supplementation (180 mg/day) for 12 weeks in patients with T2DM and Alzheimer's disease resulted in a significant reduction in HOMA-IR. In another RCT reported by Yaikwawong et al., supplementation of curcumin (1500 mg/day) for 12 months significantly decreased the levels of HOMA-IR, FBS and glycosylated haemoglobin (HbA1c) in T2DM patients (54). In an RCT, Karandish et al. showed that supplementation with curcumin (500 mg) significantly increased fasting plasma glucose (FPG), 2-hour postprandial glucose (2-hpp), HbA1c, insulin levels, and total insulin sensitivity in overweight or obese subjects with prediabetes (55). Furthermore, Mokhtari et al. showed that diabetic foot ulcer patients who were supplemented with nanocurcumin (80 mg/day) for 12 weeks had significant reductions in FPG and HOMA-IR levels (56).

Glucagon-like peptide-1 (GLP-1) is a glucoincretin hormone produced in enteroendocrine cells of the gut and released upon food intake. This hormone promotes the secretion of insulin from pancreatic beta cells (57). Kato et al. (58) demonstrated that administration of curcumin (1.5 mg/kg) to Sprague-

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

Dawley rats improved glucose tolerance by increasing the secretion of glucagon-like peptide-1 (GLP-1). Moreover, Seo et al. reported that curcumin supplementation (0.02%, w/w) significantly reduced HbA1c and HOMA-IR levels in diabetic db/db mice. Moreover, curcumin suppressed the activities of G6Pase and PEPCK (59). Besides, curcumin was shown to significantly decrease the hepatic mRNA expression levels of glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK) in diet-induced obese (DIO) mice (60).

Other factors that lead to reduced insulin sensitivity include interleukin-1 beta (IL-1β) and tumour necrosis factor alpha (TNF-α) (61). NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) upregulates expression of IL-1β and TNF-α (62). One important pathway that leads to NF-κB activation is the toll-like receptor 4 (TLR4) pathway (63). These factors are inhibited by the expression and activity of curcumin (52, 64).

Table 1 presents the relationship between curcumin and carbohydrate metabolism in preclinical studies, whereas Table 2 summarises the RCT studies.

Table 1. Published studies on the relationship between curcumin and sugar metabolism in preclinical phase.

Study	Dosage	Cellular or molecular mechanism	Effects on glycemic variables	Study model
(60)	40 mg/kg 80 mg/kg	G6pase, PEPCK ↓	-	DIO mice
(66)	100 mg/kg	AMPK ↑	Glu ↓	Diabetic rats
(58)	1.5 mg/kg	Glucose tolerance ↑	GLP-1 ↑	Sprague-Dawley rats
(36)	-	α-C, TNF-FFAs, LDL ↓	FBG ↓	T2DM rat models
(37)	100, 200, 400 mg/kg	R1-IGF, IRS-2, PI3K, p-PI3K, Akt, p-Akt ↑	-	APPswe/PS1dE9 mice
(52)	200 mg/kg	B, TLR4κ-NFα, -TNF ↓	Glu, HOMA-IR ↓	T2DM rats
(44)	100 mg/kg	γPPARα, PPAR ↑ Bκ-NFα, -TNF ↓	Glu ↓	HFD rats
(64)	-	Bκ-NF, IL-1β, α-TNF ↓	Insulin ↑ Glu ↓	Diabetic rats
(47)	10 μM	p38, AMPK, Glucose absorption ↑	-	Rat L6 myotubes
(48)	50 mg/kg	PC, cAMP/PKA Gluconeogenesis ↓ PDH ↑	FBG ↓	HFD mice
(49)	25 μM	G6pase, PEPCK, Gluconeogenesis ↓ AMPK ↑	-	Liver of C57/BL6J mice

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

(59)	0.02% w/w	G6pase, PEPCK, FFAs, cholesterol ↓	HOMA-IR, HbA1c ↓	Diabetic db/db mice

DIO: diet-induced obesity, T2DM: type 2 diabetes mellitus, HFD: high-fat diet

Table 2. Published RCT studies on the relationship between curcumin and sugar metabolism.

Study	Dosage	Cellular or molecular mechanism	Effects on glycemic variables	Study model
(67)	500 mg	-	FBG ↓	PCOS patients
(68)	250 mg	Adiponectin ↑	HOMA-IR, FBG, OGTT ↓ HbA1c	T2DM patients
(69)	200 mg	-	HOMA-IR ↓	Subjects with suboptimal values of FPG
(70)	1000 mg	-	FBG ↓	PCOS patients
(71)	500 mg	-	HOMA-IR ↓	Rheumatoid arthritis patients
(54)	1500 mg	Adiponectin ↑	HOMA-IR, FBS, HbA1c ↓	T2DM patients
(55)	500 mg	-	FBG, 2hpp, HbA1c ↓ insulin ↑	Overweight or obese prediabetic subjects
(72)	500 mg	FFAs ↓	FBS, HbA1c ↓	Patients with nonalcoholic simple fatty liver disease
(73)	500 mg	PPARγ ↑	FBG, HOMA-IR ↓	PCOS patients
(74)	400 mg	-	FBG ↓	Individuals with obesity
(75)	70 mg	-	FBS, HbA1c ↓	NAFLD patients
(76)	250 mg	Adiponectin ↑	HOMA-IR ↓	T2DM patients
(77)	80 mg	-	FBG ↓	Patients with diabetes

PCOS: polycystic ovary syndrome, NAFLD: non-alcoholic fatty liver disease

Conclusion

Curcumin is a bioactive compound with unique molecular structure, biological properties and bioavailability. Its therapeutic efficacy varies with the dose and duration of administration. Curcumin is also prone to decomposition under different conditions such as light, temperature and pH variations. Furthermore, the curcumin nanoformulation is suggested as a novel therapeutic strategy to enhance the clinical efficacy of

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

curcumin. Preclinical studies and RCTs have demonstrated that curcumin is associated with mediators that influence carbohydrate metabolism. These studies showed that this compound improves glycaemic control and metabolic indices through its effects on GLP-1, lipid metabolism and inflammatory mediators. Preclinical studies have laid a basis for understanding the effects of curcumin on human glucose metabolism. In human studies, oral curcumin doses ranging from 70 to 1500 mg/day have been used to improve glucose metabolism. It is unlikely that the poor bioavailability of curcumin will be of much concern. However, it should be noted that the long-term administration of high doses of curcumin may cause adverse effects, which could potentially reduce its therapeutic efficacy.

Long-term use of high-dose curcumin may be associated with impaired wound healing, decreased cell proliferation, increased cellular stress, DNA damage and apoptosis (65). So the possible side effects of high-dose curcumin should be further studied at preclinical and clinical phases. In future studies, animal and human studies can be performed to compare the improvement in carbohydrate metabolism at different doses and side effects of this compound. These findings indicate that future investigations can conduct systematic studies and meta-analyses to investigate the association between curcumin and glucose metabolism.

Funding

Authors had received no financial support for this article.

CRediT authorship contribution statement

Conceptualization: ANA, MK, Methodology, Validation: NES, Formal Analysis, Investigation, Resources: FB, RD, Software, Data Curation: DQ, Writing–Original Draft Preparation, Writing–Review & Editing, Visualization, Supervision, Project Administration: ANA, DQ.

Declaration of Generative AI and AI-assisted technologies in the writing process

No artificial intelligence tools were used to write the article.

Conflict of interest

The authors declare no competing interests.

Ethical considerations

The work in this paper used only previously published literature and did not involve human participants, animals, clinical data or personally identifiable information. Thus, ethical approval and informed consent were not required for this review study based on the institutional and international guidelines for research ethics.

Data availability statement

This study is a narrative review article that does not have specific data.

Acknowledgements

The authors thank Dr. Mostafa Vaghar Tabari for the final English editing of this article.

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

References

1. Niaz K, Khan F, Shah MA. Analysis of carbohydrates (monosaccharides, polysaccharides). Recent advances in natural products analysis: Elsevier; 2020. p. 621-33. https://doi.org/10.1016/B978-0-12-816455-6.00018-4.
2. Manfredi AP, Pisa JH, Valdeón DH, Perotti NI, Martínez MA. Synergistic effect of simple sugars and carboxymethyl cellulose on the production of a cellulolytic cocktail from Bacillus sp. AR03 and enzyme activity characterization. Applied Biochemistry and Biotechnology. 2016;179:16-32. https://doi.org/10.1007/s12010-015-1976-5.
3. Andevari AN, Moein S, Qujeq D, Moazezi Z, Hajian-Tilaki K. The Effects of Atorvastatin Consumption on Biochemical Variables in Patients with Type 2 Diabetes Mellitus and Pre-diabetes. International Journal of Medical Laboratory. 2022. https://doi.org/10.18502/ijml.v9i3.10905.
4. Andevari AN, Moein S, Qujeq D, Moazezi Z, Tilaki KH. Effects of atrovastatin on concentrations of 3-hydroxy-3-methylglutaryl-coenzyme A-reductase (HMG-CoA-R), proprotein convertase subtilisin/kexin type 9 (PCSK9) and sortilin in patients with type 2 diabetes mellitus and pre-diabetics. Journal of Nephropathology. 2020;10(1):e05-e. https://doi.org/ 10.34172/jnp.2021.05.
5. Andevari AN, Moein S, Qujeq D, Moazezi Z, Tilaki KH. The effect of atorvastatin on the concentrations of methylglyoxal, glyoxalase 1, and aldo–keto reductase family 1 member B10 in patients with type 2 diabetes mellitus and prediabetes. International Journal of Diabetes in Developing Countries. 2024;44(2):400-8. https://doi.org/10.1007/s13410-023-01249-6.
6. 6. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. Nature reviews Disease primers. 2019;5(1):41. https://doi.org/10.1038/s41572-019-0092-1.
7. Andevari AN, Firoozjaee AH, Meftah N, Asciabari HA, Bahri F, Shahandashti NE, et al. The effects of atorvastatin consumption on blood levels of sortilin, glycemic, and lipid indices in type 2 diabetic patients: A randomized clinical trial. International Journal of Diabetes in Developing Countries. 2025:1-8. https://doi.org/10.1007/s13410-025-01557-z.
8. Abd El-Hack ME, El-Saadony MT, Swelum AA, Arif M, Abo Ghanima MM, Shukry M, et al. Curcumin, the active substance of turmeric: its effects on health and ways to improve its bioavailability. Journal of the Science of Food and Agriculture. 2021;101(14):5747-62. https://doi.org/10.1002/jsfa.11372.
9. Feng J-Y, Liu Z-Q. Phenolic and enolic hydroxyl groups in curcumin: which plays the major role in scavenging radicals? Journal of agricultural and food chemistry. 2009;57(22):11041-6. https://doi.org/10.1021/jf902244g.
10. Kocaadam B, Şanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Critical reviews in food science and nutrition. 2017;57(13):2889-95. https://doi.org/10.1080/10408398.2015.1077195.
11. Patra D, El Kurdi R. Curcumin as a novel reducing and stabilizing agent for the green synthesis of metallic nanoparticles. Green Chemistry Letters and Reviews. 2021;14(3):474-87. https://doi.org/10.1080/17518253.2021.1941306.
12. Esatbeyoglu T, Huebbe P, Ernst IM, Chin D, Wagner AE, Rimbach G. Curcumin—from molecule to biological function. Angewandte Chemie International Edition. 2012;51(22):5308-32. https://doi.org/10.1002/anie.201107724.
13. Klawitter M, Quero L, Klasen J, Gloess AN, Klopprogge B, Hausmann O, et al. Curcuma DMSO extracts and curcumin exhibit an anti-inflammatory and anti-catabolic effect on human intervertebral disc cells, possibly by influencing TLR2 expression and JNK activity. Journal of Inflammation. 2012;9:1-14. http://www.journal inflammation.com/content/9/1/29.
14. Kharat M, Du Z, Zhang G, McClements DJ. Physical and chemical stability of curcumin in aqueous solutions and emulsions: impact of pH, temperature, and molecular environment. Journal of agricultural and food chemistry. 2017;65(8):1525-32. https://doi.org/10.1021/acs.jafc.6b04815.
15. Syed HK, Liew KB, Loh GOK, Peh KK. Stability indicating HPLC–UV method for detection of curcumin in Curcuma longa extract and emulsion formulation. Food Chemistry. 2015;170:321-6. https://doi.org/10.1016/j.foodchem.2014.08.066.
16. Zhu J. Curcumin and its oxidative degradation products: their comparative effects on inflammation. 2016. https://doi.org/ 10.7275/8433277.
17. Niu Y, Ke D, Yang Q, Wang X, Chen Z, An X, et al. Temperature-dependent stability and DPPH scavenging activity of liposomal curcumin at pH 7.0. Food Chemistry. 2012;135(3):1377-82. https://doi.org/10.1016/j.foodchem.2012.06.018.
18. Wu Y, Mou B, Song S, Tan C-P, Lai O-M, Shen C, et al. Curcumin-loaded liposomes prepared from bovine milk and krill phospholipids: Effects of chemical composition on storage stability, in-vitro digestibility and anti-hyperglycemic properties. Food Research International. 2020;136:109301. https://doi.org/10.1016/j.foodres.2020.109301.
19. Saikeaw R, Bijaisoradat O, Netcharoensirisuk P, Dubas ST. Improved pH sensing of curcumin loaded polyelectrolyte multilayers thin films. Sensor Letters. 2016;14(6):572-6. https://doi.org/10.1166/sl.2016.3634.
20. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Molecular pharmaceutics. 2007;4(6):807-18. https://doi.org/10.1021/mp700113r.
21. Sabet S, Rashidinejad A, Melton LD, McGillivray DJ. Recent advances to improve curcumin oral bioavailability. Trends in Food Science & Technology.

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

2021;110:253-66. https://doi.org/10.1016/j.tifs.2021.02.006.
22. Gera M, Sharma N, Ghosh M, Lee SJ, Min T, Kwon T, et al. Nanoformulations of curcumin: an emerging paradigm for improved remedial application. Oncotarget. 2017;8(39):66680. https://doi.org/ 10.18632/oncotarget.19164.
23. Hafez Ghoran S, Calcaterra A, Abbasi M, Taktaz F, Nieselt K, Babaei E. Curcumin-based nanoformulations: A promising adjuvant towards cancer treatment. Molecules. 2022;27(16):5236. https://doi.org/10.3390/molecules27165236.
24. Gorgani L, Mohammadi M, Najafpour GD, Nikzad M. Piperine—the bioactive compound of black pepper: from isolation to medicinal formulations. Comprehensive reviews in food science and food safety. 2017;16(1):124-40. https://doi.org/10.1111/1541-4337.12246.
25. Askari G, Sahebkar A, Soleimani D, Mahdavi A, Rafiee S, Majeed M, et al. The efficacy of curcumin-piperine co-supplementation on clinical symptoms, duration, severity, and inflammatory factors in COVID-19 outpatients: a randomized double-blind, placebo-controlled trial. Trials. 2022;23(1):472. https://doi.org/10.1186/s13063-022-06375-w.
26. Soliman G. Effect of curcumin, mixture of curcumin and piperine and curcum (turmeric) on lipid profile of normal and hyperlipidemic rats. The Egyptian Journal of Hospital Medicine. 2005;21(1):145-61. https://doi.org/ 10.21608/ejhm.2005.18057.
27. Hosseini H, Bagherniya M, Sahebkar A, Iraj B, Majeed M, Askari G. The effect of curcumin-piperine supplementation on lipid profile, glycemic index, inflammation, and blood pressure in patients with type 2 diabetes mellitus and hypertriglyceridemia. Phytotherapy Research. 2024;38(11):5150-61. https://doi.org/10.1002/ptr.8304.
28. Hoehle SI, Pfeiffer E, Sólyom AM, Metzler M. Metabolism of curcuminoids in tissue slices and subcellular fractions from rat liver. Journal of agricultural and food chemistry. 2006;54(3):756-64. https://doi.org/10.1021/jf058146a.
29. Schalkwijk CG, Micali LR, Wouters K. Advanced glycation endproducts in diabetes-related macrovascular complications: focus on methylglyoxal. Trends in Endocrinology & Metabolism. 2023;34(1):49-60. https://doi.org/10.1016/j.tem.2022.11.004.
30. Brunham LR, Kruit JK, Pape TD, Timmins JM, Reuwer AQ, Vasanji Z, et al. β-cell ABCA1 influences insulin secretion, glucose homeostasis and response to thiazolidinedione treatment. Nature medicine. 2007;13(3):340-7. https://doi.org/ 10.1038/nm1546.
31. Zhang C, Xiang D, Zhao Q, Jiang S, Wang C, Yang H, et al. Curcumin nicotinate decreases serum LDL cholesterol through LDL receptor-mediated mechanism. European Journal of Pharmacology. 2022;931:175195. https://doi.org/10.1016/j.ejphar.2022.175195.
32. Singh L, Sharma S, Xu S, Tewari D, Fang J. Curcumin as a natural remedy for atherosclerosis: a pharmacological review. Molecules. 2021;26(13):4036. https://doi.org/10.3390/molecules26134036.
33. Barrientos G, Sánchez-Aguilera P, Jaimovich E, Hidalgo C, Llanos P. Membrane cholesterol in skeletal muscle: a novel player in excitation-contraction coupling and insulin resistance. Journal of diabetes research. 2017;2017(1):3941898. https://doi.org/10.1155/2017/3941898.
34. Marquez VE, Blumberg PM. Synthetic diacylglycerols (DAG) and DAG-lactones as activators of protein kinase C (PK-C). Accounts of chemical research. 2003;36(6):434-43. https://doi.org/10.1021/ar020124b.
35. Gupta A, Behl T, Sehgal A, Bhardwaj S, Singh S, Sharma N, et al. Exploring the recent molecular targets for diabetes and associated complications. Molecular Biology Reports. 2021;48:2863-79. https://doi.org/10.1007/s11033-021-06294-0.
36. Su L-q, Chi H-y. Effect of curcumin on glucose and lipid metabolism, FFAs and TNF-α in serum of type 2 diabetes mellitus rat models. Saudi journal of biological sciences. 2017;24(8):1776-80. https://doi.org/10.1016/j.sjbs.2017.11.011.
37. Wang P, Su C, Feng H, Chen X, Dong Y, Rao Y, et al. Curcumin regulates insulin pathways and glucose metabolism in the brains of APPswe/PS1dE9 mice. International journal of immunopathology and pharmacology. 2017;30(1):25-43. https://doi.org/10.1177/0394632016688025.
38. Semova I, Levenson AE, Krawczyk J, Bullock K, Gearing ME, Ling AV, et al. Insulin prevents hypercholesterolemia by suppressing 12α-hydroxylated bile acids. Circulation. 2022;145(13):969-82. https://doi.org/10.1161/CIRCULATIONAHA.120.045373.
39. Shao W, Yu Z, Chiang Y, Yang Y, Chai T, Foltz W, et al. Curcumin prevents high fat diet induced insulin resistance and obesity via attenuating lipogenesis in liver and inflammatory pathway in adipocytes. PloS one. 2012;7(1):e28784. https://doi.org/10.1371/journal.pone.0028784.
40. Bassaganya-Riera J, Misyak S, Guri AJ, Hontecillas R. PPAR γ is highly expressed in F4/80hi adipose tissue macrophages and dampens adipose-tissue inflammation. Cellular immunology. 2009;258(2):138-46. https://doi.org/10.1016/j.cellimm.2009.04.003.
41. Razmpoosh E, Safi S, Nadjarzadeh A, Salehi-Abargouei A, Mazaheri M, Mirmiran P, et al. Effects of Nigella sativa supplementation on blood concentration and mRNA expression of TNF-α, PPAR-γ and adiponectin, as major adipogenesis-related markers, in obese and overweight women: a crossover, randomised-controlled trial. British Journal of Nutrition. 2023;129(4):627-36. https://doi.org/10.1017/S0007114522001428.
42. Tahri-Joutey M, Andreoletti P, Surapureddi S, Nasser B, Cherkaoui-Malki M, Latruffe N. Mechanisms mediating the regulation of peroxisomal fatty acid beta-oxidation by PPARα. International journal of molecular sciences.

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

2021;22(16):8969. https://doi.org/10.3390/ijms22168969.
43. Zheng F, Cai Y. Concurrent exercise improves insulin resistance and nonalcoholic fatty liver disease by upregulating PPAR-γ and genes involved in the beta-oxidation of fatty acids in ApoE-KO mice fed a high-fat diet. Lipids in Health and Disease. 2019;18:1-8. https://doi.org/10.1186/s12944-018-0933-z.
44. Zhao N-J, Liao M-J, Wu J-J, Chu K-X. Curcumin suppresses Notch-1 signaling: improvements in fatty liver and insulin resistance in rats. Molecular Medicine Reports. 2018;17(1):819-26. https://doi.org/10.1186/s12944-018-0933-z.
45. Demir EA, Tutuk O, Dogan-Gocmen H, Ozyilmaz DS, Karagul MI, Kara M, et al. CREB1 and PPAR-α/γ Pathways in Hepatic Ischemia/Reperfusion: Route for Curcumin to Hepatoprotection. Iranian Journal of Pharmaceutical Research: IJPR. 2023;21(1):e133779. https://doi.org/ 10.5812/ijpr-133779.
46. Gao S, Zhou J, Liu N, Wang L, Gao Q, Wu Y, et al. Curcumin induces M2 macrophage polarization by secretion IL-4 and/or IL-13. Journal of molecular and cellular cardiology. 2015;85:131-9. https://doi.org/10.1016/j.yjmcc.2015.04.025.
47. Kim JH, Park JM, Kim EK, Lee JO, Lee SK, Jung JH, et al. Curcumin stimulates glucose uptake through AMPK-p38 MAPK pathways in L6 myotube cells. Journal of Cellular Physiology. 2010;223(3):771-8. . https://doi.org/10.1002/jcp.22093.
48. Wang Z, Xu D, She L, Zhang Y, Wei Q, Aa J, et al. Curcumin restrains hepatic glucose production by blocking cAMP/PKA signaling and reducing acetyl CoA accumulation in high-fat diet (HFD)-fed mice. Molecular and cellular endocrinology. 2018;474:127-36. https://doi.org/10.1016/j.mce.2018.02.018.
49. Fujiwara H, Hosokawa M, Zhou X, Fujimoto S, Fukuda K, Toyoda K, et al. Curcumin inhibits glucose production in isolated mice hepatocytes. Diabetes research and clinical practice. 2008;80(2):185-91. https://doi.org/10.1016/j.diabres.2007.12.004.
50. Tahapary DL, Pratisthita LB, Fitri NA, Marcella C, Wafa S, Kurniawan F, et al. Challenges in the diagnosis of insulin resistance: focusing on the role of HOMA-IR and Tryglyceride/glucose index. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2022;16(8):102581. https://doi.org/10.1016/j.dsx.2022.102581.
51. Vladu IM, Forţofoiu M, Clenciu D, Forţofoiu M-C, Pădureanu R, Radu L, et al. Insulin resistance quantified by the value of HOMA-IR and cardiovascular risk in patients with type 2 diabetes. Experimental and therapeutic medicine. 2022;23(1):73. https://doi.org/10.3892/etm.2021.10996.
52. Huang J, Guan B, Lin L, Wang Y. Improvement of intestinal barrier function, gut microbiota, and metabolic endotoxemia in type 2 diabetes rats by curcumin. Bioengineered. 2021;12(2):11947-58. https://doi.org/10.1080/21655979.2021.2009322.
53. Thota RN, Rosato JI, Dias CB, Burrows TL, Martins RN, Garg ML. Dietary supplementation with curcumin reduce circulating levels of glycogen synthase kinase-3β and islet amyloid polypeptide in adults with high risk of type 2 diabetes and Alzheimer's disease. Nutrients. 2020;12(4):1032. https://doi.org/10.3390/nu12041032.
54. Yaikwawong M, Jansarikit L, Jirawatnotai S, Chuengsamarn S. Curcumin extract improves beta cell functions in obese patients with type 2 diabetes: A randomized controlled trial. Nutrition Journal. 2024;23(1):119. https://doi.org/10.1186/s12937-024-01022-3.
55. Karandish M, Mozaffari-khosravi H, Mohammadi SM, Cheraghian B, Azhdari M. The effect of curcumin and zinc co-supplementation on glycemic parameters in overweight or obese prediabetic subjects: A phase 2 randomized, placebo-controlled trial with a multi-arm, parallel-group design. Phytotherapy Research. 2021;35(8):4377-87. https://doi.org/10.1002/ptr.7136.
56. Mokhtari M, Razzaghi R, Momen-Heravi M. The effects of curcumin intake on wound healing and metabolic status in patients with diabetic foot ulcer: A randomized, double-blind, placebo-controlled trial. Phytotherapy Research. 2021;35(4):2099-107. https://doi.org/10.1002/ptr.6957.
57. Tomas E, Habener JF. Insulin-like actions of glucagon-like peptide-1: a dual receptor hypothesis. Trends in Endocrinology & Metabolism. 2010;21(2):59-67. https://doi.org/ 10.1016/j.tem.2009.11.007.
58. Kato M, Nishikawa S, Ikehata A, Dochi K, Tani T, Takahashi T, et al. Curcumin improves glucose tolerance via stimulation of glucagon-like peptide-1 secretion. Molecular Nutrition & Food Research. 2017;61(3):1600471. https://doi.org/10.1002/mnfr.201600471.
59. Seo KI, Choi MS, Jung UJ, Kim HJ, Yeo J, Jeon SM, et al. Effect of curcumin supplementation on blood glucose, plasma insulin, and glucose homeostasis related enzyme activities in diabetic db/db mice. Molecular nutrition & food research. 2008;52(9):995-1004. https://doi.org/10.1002/mnfr.200700184.
60. Ding L, Li J, Song B, Xiao X, Zhang B, Qi M, et al. Curcumin rescues high fat diet-induced obesity and insulin sensitivity in mice through regulating SREBP pathway. Toxicology and applied pharmacology. 2016;304:99-109. https://doi.org/10.1016/j.taap.2016.05.011.
61. Uzokov J, Alyavi B, Payziev D, Abdullaev A, Muxitdinova O. Influence of diet with low glycemic index on pro-inflammatory cytokines in patients with metabolic syndrome and coronary artery disease. Atherosclerosis. 2021;331:e250. https://doi.org/ 10.1016/j.atherosclerosis.2021.06.764.
62. Andevari AN, Qujeq D. Anti-inflammatory Mechanisms Beyond Cholesterol-Lowering Capabilities of Statins: Evidence from in vitro and in vivo Studies. Advances in Pharmacology and Therapeutics Journal. 2025.
63. Palideh A, Vaghari-Tabari M, Andevari AN, Qujeq D, Asemi Z, Alemi F, et al. MicroRNAs and Periodontal Disease: Helpful Therapeutic Targets? Advanced

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]

Pharmaceutical Bulletin. 2022;13(3):423. https://doi.org/ 10.34172/apb.2023.048.
64. Zamanian MY, Alsaab HO, Golmohammadi M, Yumashev A, Jabba AM, Abid MK, et al. NF-κB pathway as a molecular target for curcumin in diabetes mellitus treatment: Focusing on oxidative stress and inflammation. Cell Biochemistry and Function. 2024;42(4):e4030. https://doi.org/10.1002/cbf.4030.
65. Moghaddam NSA, Oskouie MN, Butler AE, Petit PX, Barreto GE, Sahebkar A. Hormetic effects of curcumin: What is the evidence? Journal of cellular physiology. 2019;234(7):10060-71.
66. Soetikno V, Sari FR, Sukumaran V, Lakshmanan AP, Harima M, Suzuki K, et al. Curcumin decreases renal triglyceride accumulation through AMPK–SREBP signaling pathway in streptozotocin-induced type 1 diabetic rats. The Journal of nutritional biochemistry. 2013;24(5):796-802. https://doi.org/10.1016/j.jnutbio.2012.04.013.
67. Heshmati J, Moini A, Sepidarkish M, Morvaridzadeh M, Salehi M, Palmowski A, et al. Effects of curcumin supplementation on blood glucose, insulin resistance and androgens in patients with polycystic ovary syndrome: A randomized double-blind placebo-controlled clinical trial. Phytomedicine. 2021;80:153395. https://doi.org/10.1016/j.phymed.2020.153395.
68. Chuengsamarn S, Rattanamongkolgul S, Luechapudiporn R, Phisalaphong C, Jirawatnotai S. Curcumin extract for prevention of type 2 diabetes. Diabetes care. 2012;35(11):2121-7. https://doi.org/10.2337/dc12-0116.
69. Cicero AF, Sahebkar A, Fogacci F, Bove M, Giovannini M, Borghi C. Effects of phytosomal curcumin on anthropometric parameters, insulin resistance, cortisolemia and non-alcoholic fatty liver disease indices: a double-blind, placebo-controlled clinical trial. European journal of nutrition. 2020;59:477-83. https://doi.org/10.1007/s00394-019-01916-7.
70. Ghanbarzadeh-Ghashti N, Ghanbari-Homaie S, Shaseb E, Abbasalizadeh S, Mirghafourvand M. The effect of Curcumin on metabolic parameters and androgen level in women with polycystic ovary syndrome: a randomized controlled trial. BMC Endocrine Disorders. 2023;23(1):40. https://doi.org/10.1186/s12902-023-01295-5.
71. Pourhabibi-Zarandi F, Rafraf M, Zayeni H, Asghari-Jafarabadi M, Ebrahimi AA. Effects of curcumin supplementation on metabolic parameters, inflammatory factors and obesity values in women with rheumatoid arthritis: A randomized, double-blind, placebo-controlled clinical trial. Phytotherapy Research. 2022;36(4):1797-806. https://doi.org/10.1002/ptr.7422.
72. He Y, Chen X, Li Y, Liang Y, Hong T, Yang J, et al. Curcumin supplementation alleviates hepatic fat content associated with modulation of gut microbiota-dependent bile acid metabolism in patients with nonalcoholic simple fatty liver disease: A randomized controlled trial. The American Journal of Clinical Nutrition. 2024;120(1):66-79. https://doi.org/10.1016/j.ajcnut.2024.05.017.
73. Jamilian M, Foroozanfard F, Kavossian E, Aghadavod E, Shafabakhsh R, Hoseini A, et al. Effects of curcumin on body weight, glycemic control and serum lipids in women with polycystic ovary syndrome: A randomized, double-blind, placebo-controlled trial. Clinical nutrition ESPEN. 2020;36:128-33. https://doi.org/10.1016/j.clnesp.2020.01.005.
74. Hellmann PH, Bagger JI, Carlander KR, Forman J, Chabanova E, Svenningsen JS, et al. The effect of curcumin on hepatic fat content in individuals with obesity. Diabetes, Obesity and Metabolism. 2022;24(11):2192-202. https://doi.org/10.1111/dom.14804.
75. Rahmani S, Asgary S, Askari G, Keshvari M, Hatamipour M, Feizi A, et al. Treatment of non-alcoholic fatty liver disease with curcumin: A randomized placebo-controlled trial. Phytotherapy Research. 2016;30(9):1540-8. https://doi.org/10.1002/ptr.5659.
76. Chuengsamarn S, Rattanamongkolgul S, Phonrat B, Tungtrongchitr R, Jirawatnotai S. Reduction of atherogenic risk in patients with type 2 diabetes by curcuminoid extract: a randomized controlled trial. The Journal of nutritional biochemistry. 2014;25(2):144-50. https://doi.org/10.1016/j.jnutbio.2013.09.013.
77. Shafabakhsh R, Asemi Z, Reiner Ž, Soleimani A, Aghadavod E, Bahmani F, et al. The effects of nano-curcumin on metabolic status in patients with diabetes on hemodialysis, a randomized, double blind, placebo-controlled trial. Iranian Journal of Kidney Diseases. 2020;14(4).

[Downloaded from jbrms.medilam.ac.ir on 2026-10-07]